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(21) International Application Number: PCT/US98/27406 (22) International Filing Date: 23 December 1998 (23.12.98) (30) Priority Data: 08/998,877 24 December 1997 (24.12.97) US (71) Applicant: SRI INTERNATIONAL [US/US]; 333 Ravenswood Avenue, Menlo Park, CA 94025 (US). (72) Inventors: TANABE, Masato; 972 Moreno, Palo Alto, CA 94303 (US). PETERS, Richard, H.; 365 Springpark Circle, San Jose, CA 95136 (US). CHAO, Wan-Ru; 1510 Oriole Avenue, Sunnyvale, CA 94087 (US). JONG, Ling; 681 Endicott Drive, Sunnyvale, CA 94087 (US). (74) Agents: REED, Dianne, E. et al.; Reed & Associates, 3282 Alpine Road, Portola Valley, CA 94028 (US).	(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Eurasian patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 23 December 1999 (23.12.99)	
(54) Title: NOVEL ANTI-ESTROGENIC STEROIDS, AND ASSOCIATED PHARMACEUTICAL COMPOSITIONS AND METHODS OF USE		
(57) Abstract Novel anti-estrogenic compounds are provided which are useful to treat a variety of disorders, particularly estrogen-dependant disorders. Preferred compounds have 1,3,5-estratriene nucleus, and are substituted at the C-17 or C-11 position with a molecular moiety which renders the compounds effective to competitively block the binding of estrogen to its receptor. Particularly preferred compounds are 17-desoxy-1,3,5-estratrienes. Therapeutic methods and pharmaceutical compositions are provided as well.		

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PCT/US 98/27406

page 1 of 7

INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 98/27406

C/(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 318 917 A (W. R. BENN ET AL) 9 May 1967 (1967-05-09) page 2, line 29 - line 37; examples 9-14 ---	8-10, 14-16, 23-36,41
A	US 3 448 126 A (BENN WALTER R) 3 June 1969 (1969-06-03) column 3, line 38 - line 43; claim 1 ---	8-10, 14-16, 23-36,41
A	WO 93 13123 A (ROUSSEL UCLAF) 8 July 1993 (1993-07-08) the whole document, in particular page 17, paragraph 3-4 and pages 67-68 ---	8-10, 14-19, 23-36,41
A	US 3 271 428 A (F. J. VILLANI ET AL) 6 September 1966 (1966-09-06) column 2, line 58 - line 68; examples 1,2,5 ---	8-10, 14-19, 23-36,41
X	S. MIYAIRI ET AL: "Structure of the Adduct of 16.alpha.-hydroxysterone with a Primary Amine: Evidence for the Heyns Rearrangement of Steroidal D-Ring alpha-Hydroxyimines" STERIODS: STRUCTURE, FUNCTION, AND REGULATION., vol. 56, no. 7, July 1991 (1991-07), pages 361-366, XP002109814 ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY., US ISSN: 0039-128X compounds 1 and 3 on page 363 ---	14
X	US 3 536 703 A (COLTON FRANK B ET AL) 27 October 1970 (1970-10-27) column 2, line 56 - line 67; example 8 ---	8,14,41
X	R. CONSUELO ET AL: "Effects of 17.beta.-(N,N-Diethylaminethyl)-amino-1,3, 5(10)-estratrien-3-ol, and its Androstane Analog on Blood Clotting Time" MEDICINAL CHEMISTRY RESEARCH, vol. 7, no. 2, February 1997 (1997-02), pages 67-75, XP002109815 compound 1a on page 68 ---	14
X	US 3 716 530 A (KRUBINER A ET AL) 13 February 1973 (1973-02-13) example 4 ---	8,14

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INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 98/27406

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR 3 012 M (ROUSSEL-UCLAF) 21 December 1964 (1964-12-21) compound III on page 4 ---	14
X	US 2 666 769 A (F. B. COLTON) 19 January 1954 (1954-01-19) column 3, line 33 - line 45 ---	8, 14
A	BLICKENSTAFF, ROBERT T. ET AL: "Synthesis of some analogs of estradiol" STERIODS., vol. 46, no. 4/5, November 1985 (1985-11), XP002109816 ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY., US page 897, compounds 19 and 23 and page 898; table 2 ---	14
A	DATABASE WPI Section Ch, Derwent Publications Ltd., London, GB; Class B00, AN 66-33967F XP002109827 & JP 43 021058 B (DAINIPPON SEIYAKU KK) abstract ---	8, 14, 23-36, 41
X	US 2 840 581 A (J. HOGG ET AL) 24 June 1958 (1958-06-24) column 1, line 35 - line 52; examples 4-6, 13-15, 17-19 ---	8, 14, 28-30, 33, 35, 36, 41
A	DE 23 61 120 A (AKZO NV) 12 June 1974 (1974-06-12) page 4, paragraph 2 - paragraph 3; examples 5, 6 ---	8-10, 17-19, 23-36, 41
A	EP 0 471 612 A (ROUSSEL UCLAF) 19 February 1992 (1992-02-19) page 42 - page 43; example 14 page 11, line 2 - line 8 ---	8-10, 17-19, 23-36, 41
A	EP 0 546 591 A (SCHERING AG) 16 June 1993 (1993-06-16) the whole document, in particular page 2, lines 50-52 ---	8-10, 17-19, 23-36, 41

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INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 98/27406

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 405 147 A (COUNSELL RAYMOND E ET AL) 8 October 1968 (1968-10-08) column 2, line 24 - line 31; examples 7-9	20, 28, 30, 31, 33, 35, 36, 41
A	STRECKE, J. ET AL: "Animal experiments on the estrogenic and antiestrogenic effects of 17.alpha.-thiocyanomethyl-17.beta.-tetrahydropranyloxyestra-1,3,5(10)-triene-3-methylether and 17.beta.-phenylaminocarbonyloestra-1,3,5(10)-triene-3-methylether" PHARMAZIE, vol. 32, no. 10, October 1997 (1997-10), pages 598-602, XP002109817 BERLIN DE compound 1 on page 598, column 1	11, 23-25, 30-36, 41
A	WO 96 03995 A (HOLICK MICHAEL F) 15 February 1996 (1996-02-15) page 5, line 1 - line 6; claim 9	11-13, 20, 23-36, 41
A	CHEMICAL ABSTRACTS, vol. 76, no. 21, 22 May 1972 (1972-05-22) Columbus, Ohio, US; abstract no. I22090, AGRESTA, G. ET AL: "Biological activities of a new acetalic ether of estradiol, 17.beta.-(1',4'-dioxan-2'-yloxy)-estra-1,3,5(10)-trien-3-ol (17-dioxanylestradiol)" page 83; column 1; XP002109825 abstract & ACTA ENDOCRINOL. (COPENHAGEN) (1972), 69(1), 95-106 , ---	11-13, 20, 23-36
A	H BRUNNER ET AL: "Synthese und Antitumoraktivität von cis-Dichloroplatin(II) -Komplexen mit Östradiolderivaten" MONATSHEFTE FÜR CHEMIE, vol. 124, no. 1, 1 January 1993 (1993-01-01), pages 83-102, XP002089839 ISSN: 0026-9247 page 98, compounds 13, 14; page 90, paragraph 4; page 91; table 2; page 92, paragraph 3 - page 93, paragraph 1 ---	11-13, 20, 23-36, 41
	--- -/--	

INTERNATIONAL SEARCH REPORT

national Application No
PCT/US 98/27406

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 431 258 A (LEFEBVRE YVON ET AL) 4 March 1969 (1969-03-04) example 2 ----	11,20
A	US 3 271 392 A (Y. LEFEBVRE) 6 September 1966 (1966-09-06) the whole document, in particular column 1, lines 34-50 ----	11-13, 23-36,41
X	BE 661 288 A (ROUSSEL-UCLAF) 20 September 1965 (1965-09-20) page 3, paragraph 2 - paragraph 4; example 1 ----	11,20, 30,41
A	EL GARROUJ, DRISS ET AL: "Steroidal Affinity Labels of the Estrogen Receptor 2.17 alpha-(Haloacetamido)alkyl estradiols" JOURNAL OF MEDICINAL CHEMISTRY., vol. 38, no. 13, 23 June 1995 (1995-06-23), pages 2339-2348, XP002109818 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623 page 2341, compounds 19,21,23 page 2341, column 2, paragraph 2 page 2342: table 1 ----	11,20, 23-36,41
A	ALIAU, SIGRID ET AL: "17.alpha.-(Haloacetamidoalkyl)estradiols alkylate the human estrogen receptor at cysteine residues 417 and 530" BIOCHEMISTRY., vol. 36, no. 19, 13 May 1997 (1997-05-13), pages 5861-5867, XP002109819 AMERICAN CHEMICAL SOCIETY. EASTON, PA., US ISSN: 0006-2960 page 5862, column 1, compounds 2B, 3B, 3I and figure 1 page 5864, column 2, paragraph 2 ----	11,20, 23-36,41
A	US 3 946 052 A (CROWE DAVID F ET AL) 23 March 1976 (1976-03-23) the whole document ----	11,20, 23-36,41
A	F. KINCL: "Notiz über den Mechanismus der Anti-Ovulation mit 6-Chloro-delta-6-17.alpha.-Acetoxyprogeste ron in Kaninchen" ENDOKRINOLOGIE, vol. 44, no. 1/2, 1963, pages 67-71, XP002109820 LEIPZIG, DE the whole document, in particular page 69; table II ----- -/--	37

INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 98/27406

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	F. KINCL ET AL: "Antifertility Activity of Various Steroids in the Female Rat" JOURNAL OF REPRODUCTION AND FERTILITY, vol. 10, 1965, pages 105-113, XP002109821 OXFORD, GB page 108; table 3 ---	37
A	US 3 766 171 A (MARX A ET AL) 16 October 1973 (1973-10-16) column 2, line 15 - line 21; example 15 ---	38
A	CHEMICAL ABSTRACTS, vol. 114, no. 10, 11 March 1991 (1991-03-11) Columbus, Ohio, US; abstract no. 88501, BASU, KRISHNAKALI ET AL: "Effects of 3-hydrazone modification on the metabolism and protein binding of progesterone" page 429; column 2; XP002109826 abstract & INT. J. PHARM. (1990), 65(1-2), 109-14 , ---	38
A	WO 97 22618 A (VERTEX PHARMA) 26 June 1997 (1997-06-26) page 30, paragraph 1 ---	38
X	US 5 554 603 A (KIM HYUN K ET AL) 10 September 1996 (1996-09-10) column 15, line 16 - line 19; figure 4 ---	39
Y		39
X	WO 87 00175 A (STANFORD RES INST INT) 15 January 1987 (1987-01-15) page 28, line 15 - line 21; examples 1-9 page 31, line 12 - line 18 page 32, line 22 - page 33, line 10 ---	39
Y		39
Y	PETERS, RICHARD H. ET AL: "11.beta.-Nitrate estrane analogs: potent estrogens" JOURNAL OF MEDICINAL CHEMISTRY, vol. 32, no. 10, October 1989 (1989-10), pages 2306-2310, XP002109822 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623 the whole document ---	39
P,X	WO 98 07740 A (SCHERING AG) 26 February 1998 (1998-02-26) page 15, paragraph 2; example 30 ---	39
Y	US 3 318 925 A (G. ANNER ET AL) 9 May 1967 (1967-05-09) example 1 ---	40

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/27406

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	N. PEMMARAJU ET AL: "Preparative chemical methods for aromatisation of 19-nor-delta-4,-3-oxosteroids" STEROIDS., vol. 59, no. 11, November 1994 (1994-11), pages 621-627, XP002109823 ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY., US page 624; table 2	40
Y	SUN-SHINE YUAN: "Synthesis of 3,4-13C2 Steroids" STEROIDS., vol. 39, no. 3, March 1982 (1982-03), pages 279-289, XP002109824 ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY., US page 288, paragraph 2	40
Y	US 3 859 365 A (YOUNG DAVID A) 7 January 1975 (1975-01-07) the whole document	40

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 27406

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 23-39
is(are) directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. ☒ Claims Nos.: 1-7
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
See further information sheet
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see further information sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☒ The additional search fees were accompanied by the applicant's protest.☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 1.2

Claims Nos.: 1-7

Claims 1-7 attempt to define the subject matter of the claimed invention in terms of a result to be achieved, claims 1-3 in particular give no structural features of the claimed compounds AT ALL, but rather define them in terms of their anti-estrogenic effects and low estrogenic activity. Claims 4-7 further specify two very trivial structural features, namely the *estra-1,3,5(10)-triene* structure and the *17-desoxy* derivative thereof. These per se are well known structural features and give no distinction of the claimed subject matter over the state of the art, consequently the (allegedly) distinguishing feature of each of these claims is their function as anti-estrogens with low estrogenic activity as measured by a well known technique. This is also the problem to be solved by the claimed compounds (see page 5, lines 10-13 of the description). Consequently the subject matter of claims 1-7 is entirely characterised by a desideratum, i.e. the distinguishing feature of these claims over the prior art is simply to state that they must be of such a structure that they solve the stated problem. This is a wholly unacceptable formulation from the point of view of the clarity of the claims according to Article 6 PCT, since the skilled person is given no hint whatsoever in these claims as to the technical means needed to solve the stated problem and also, for the same reason, from the standpoint of sufficiency of disclosure of these claims (Article 5 PCT), since the skilled person is at a loss as to which compounds to synthesise with any expectation of solving the problem. Consequently these claims are so unclear under Article 6 PCT and insufficiently disclosed (Article 5 PCT), that it is not possible to carry out a meaningful search thereon according to Article 17(2)(a)(ii) and (2)(b) PCT. Consequently these claims are not mentioned anywhere in the search report or in the non-unity motivation.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter 11 procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 8-10,14,23-36,41 (in part) 15,16 (in full)

Estra-1,3,5(10)-triene compounds with a cyclic substituent bound, optionally via a linker group, to position 17 of the steroid skeleton via a doubly bonded carbon or nitrogen atom, medical uses and pharmaceutical compositions thereof.

2. Claims: 8,14,23-36,41 (in part)

Estra-1,3,5(10)-triene compounds with a linear hydrocarbon substituent interrupted by at least one -O-, -S- or -NR- moiety and bound, optionally via a linker group, to position 17 of the steroid skeleton via a doubly bonded carbon or nitrogen atom, medical uses and pharmaceutical compositions thereof.

3. Claims: 8-10,23-36,41 (in part) 17-19 (in full)

Estra-1,3,5(10)-triene compounds substituted in position 11 by a doubly bound carbon or nitrogen atom, medical uses and pharmaceutical compositions thereof.

4. Claims: 11,20,23-36,41 (in part) 12,13,21,22 (in full)

17-Desoxy-estra-1,3,5(10)-triene compounds with a cyclic substituent bound, optionally via a linker group, to position 17 of the steroid skeleton via a singly bonded carbon atom, medical uses and pharmaceutical compositions thereof.

5. Claims: 11,20,23-36,41 (in part)

17-Desoxy-estra-1,3,5(10)-triene compounds with a linear hydrocarbon substituent, interrupted by at least one -O-, -S-, or -NR- moiety, bound to position 17 of the steroid skeleton via a singly bonded carbon atom, medical uses and pharmaceutical compositions thereof.

6. Claims: 37,38 (in full)

The treatment of estrogen dependent disorders using pregna-1,3,5(10)-trien-3-ol-20-one or the hydrazone thereof

7. Claim : 39 (in full)

A method for transdermal delivery of estra-1,3,5(10)-triene

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

steroids.

8. Claim : 40 (in full)

A process for the production of 7.alpha.-methyl-estrone.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/27406

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3318917 A	09-05-1967	GB 1134766 A	
US 3448126 A	03-06-1969	NONE	
WO 9313123 A	08-07-1993	FR 2685332 A AT 165365 T AU 666916 B AU 3357093 A CA 2124339 A CN 1075722 A,B DE 69225243 D DE 69225243 T EP 0623140 A ES 2115754 T FI 942944 A HU 68068 A IL 104105 A JP 7502281 T MX 9207421 A NZ 246624 A ZA 9209859 A	25-06-1993 15-05-1998 29-02-1996 28-07-1993 08-07-1993 01-09-1993 28-05-1998 29-10-1998 09-11-1994 01-07-1998 17-06-1994 29-05-1995 13-07-1997 09-03-1995 01-07-1993 21-12-1995 20-12-1993
US 3271428 A	06-09-1966	DE 1493150 A FR 4691 M GB 1043149 A NL 6407296 A US 3271426 A JP 48013111 B	07-08-1969 29-12-1964 06-09-1966 25-04-1973
US 3536703 A	27-10-1970	GB 1255840 A	01-12-1971
US 3716530 A	13-02-1973	AR 195561 A AU 4432372 A BE 787343 A DE 2237202 A FR 2149972 A GB 1365205 A JP 48028462 A NL 7209862 A ZA 7204554 A	23-10-1973 10-01-1974 09-02-1973 22-02-1973 30-03-1973 29-08-1974 14-04-1973 13-02-1973 25-04-1973
FR 3012 M		NONE	
US 2666769 A	19-01-1954	NONE	
JP 43021058 B		NONE	
US 2840581 A	24-06-1958	NONE	
DE 2361120 A	12-06-1974	NL 7216767 A NL 7315704 A AT 367067 B AT 1032373 A AU 6326373 A BE 808391 A CA 1021318 A CH 614453 A DK 293776 A,B,	11-06-1974 20-05-1975 25-05-1982 15-10-1981 05-06-1975 07-06-1974 22-11-1977 30-11-1979 30-06-1976

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/27406

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
DE 2361120	A		DK 135047 B FI 54128 B FR 2209577 A GB 1455270 A IE 38617 B JP 1289124 C JP 50029548 A JP 59033600 B PH 11191 A SE 414771 B US 3927046 A ZA 7309161 A	28-02-1977 30-06-1978 05-07-1974 10-11-1976 26-04-1978 14-11-1985 25-03-1975 16-08-1984 28-10-1977 18-08-1980 16-12-1975 30-10-1974
EP 0471612	A	19-02-1992	FR 2665901 A AT 162797 T AU 8242291 A CA 2049102 A DE 69128820 D DE 69128820 T ES 2112268 T GR 3026315 T JP 6340688 A PT 98681 A,B US 5707982 A	21-02-1992 15-02-1998 20-02-1992 15-02-1992 05-03-1998 10-06-1998 01-04-1998 30-06-1998 13-12-1994 31-07-1992 13-01-1998
EP 0546591	A	16-06-1993	DE 4132182 A AT 146185 T CA 2119780 A DE 59207687 D DK 642529 T WO 9306124 A EP 0642529 A ES 2097924 T GR 3022692 T JP 7501792 T US 5502046 A	25-03-1993 15-12-1996 01-04-1993 23-01-1997 02-06-1997 01-04-1993 15-03-1995 16-04-1997 31-05-1997 23-02-1995 26-03-1996
US 3405147	A	08-10-1968	NONE	
WO 9603995	A	15-02-1996	US 5612317 A CA 2226140 A EP 0894000 A	18-03-1997 15-02-1996 03-02-1999
US 3431258	A	04-03-1969	CH 561739 A DE 1618065 A FR 7151 M FR 1534765 A GB 1190403 A NL 6707219 A US 3398138 A	15-05-1975 25-03-1971 04-08-1969 15-05-1975 06-05-1970 27-11-1967 20-08-1968
US 3271392	A	06-09-1966	CH 463500 A DE 1568013 A FR 6863 M FR 1484102 A GB 1145336 A NL 6607840 A	05-02-1970 14-04-1969 13-09-1967 13-09-1967 15-03-1967

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/27406

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
BE 661288 A	20-09-1965	CH 435266 A	
		DE 1468902 A	23-04-1970
		DK 115110 B	08-09-1969
		FR 3851 M	
		FR 1512326 A	23-04-1968
		GB 1066301 A	
		GB 1066302 A	
		GB 1066303 A	
		NL 6503558 A	28-09-1965
		SE 320966 B	23-02-1970
		US 3291690 A	13-12-1966
US 3946052 A	23-03-1976	NONE	
US 3766171 A	16-10-1973	AT 316021 B	15-05-1974
		BE 763895 A	06-09-1971
		CA 943537 A	12-03-1974
		DE 2110523 A	16-09-1971
		DK 125643 B	19-03-1973
		FR 2085681 A	31-12-1971
		GB 1305752 A	07-02-1973
		IE 35257 B	24-12-1975
		NL 7103014 A	08-09-1971
		SE 380027 B	27-10-1975
		ZA 7101431 A	28-06-1972
WO 9722618 A	26-06-1997	US 5843904 A	01-12-1998
		AU 1465897 A	14-07-1997
		CA 2240489 A	26-06-1997
		CN 1207743 A	10-02-1999
		CZ 9801905 A	11-11-1998
		EP 0876395 A	11-11-1998
		NO 982774 A	19-08-1998
		PL 327333 A	07-12-1998
US 5554603 A	10-09-1996	AT 160573 T	15-12-1997
		AU 700576 B	07-01-1999
		AU 7728494 A	03-04-1995
		DE 69407057 D	08-01-1998
		DE 69407057 T	09-04-1998
		EP 0719276 A	03-07-1996
		ES 2110258 T	01-02-1998
		GR 3025872 T	30-04-1998
		JP 9505802 T	10-06-1997
		WO 9507925 A	23-03-1995
WO 8700175 A	15-01-1987	US 4705783 A	10-11-1987
		AT 68001 T	15-10-1991
		DE 3681786 A	07-11-1991
		DK 98087 A	25-02-1987
		EP 0227813 A	08-07-1987
		FI 870808 A,B,	25-02-1987
		JP 8016117 B	21-02-1996
		JP 63500101 T	14-01-1988
		US 4859370 A	22-08-1989
		US RE34136 E	01-12-1992
WO 9807740 A	26-02-1998	DE 19635525 A	26-02-1998

Information on patent family members

PCT/US 98/27406

Form PCT/ISA/210 (patent family annex) (July 1992)